オランザピンは化学療法の副作用をコントロールする（Abstract＃9064）

抗精神病薬は化学療法誘発性悪心･嘔吐をコントロールする

Anti-psychotic drug controls breakthrough chemotherapy-induced nausea and vomiting

従来の治療が奏効しないがん患者の化学療法誘発性悪心・嘔吐（CINV）に関する第3相試験の結果、時に衰弱をもたらすがん治療によるこの副作用に対し、抗精神病薬オランザピンが有効であるとの初めての決定的なエビデンスが示された。第48回American Society of Clinical Oncology学会で発表されたこのスタディにおいて、化学療法治療歴のない患者205人はまずガイドラインの推奨するCINV予防薬を化学療法前に投与された。これらの薬剤は多くの患者においてCINVを予防した一方で、80人においてはブレイクスルーCINVが発現した。これらの患者らはその後オランザピンまたはメトクロプラミドを毎日、3日間内服する群に無作為に割り付けられた。患者は72時間フォローされ看護師からの電話を受けたり日記を記載するよう求められた。72時間の観察期間中にオランザピン投与患者の71%（42人中30人）に嘔吐はなく、メトクロプラミド投与患者におけるその割合は32%（38人中12人）であった。オランザピンを内服した患者の67%は悪心が発現しなかったのに対し、メトクロプラミドにおけるその割合は24%であった。

Full Text

A Phase III trial in cancer patients with chemotherapy-induced nausea and vomiting (CINV) that does not respond to conventional treatments provides the first conclusive evidence that olanzapine, an anti-psychotic medication, is effective in controlling these sometimes debilitating side effects of cancer therapy. The trial was presented at the American Society of Clinical Oncology's 48th Annual Meeting.

Overall, CINV affects about 50 to 60 percent of patients taking certain types of chemotherapy. While these side effects can usually be controlled with available medications, a significant minority of patients, about 30 to 40 percent, experience "breakthrough" CINV, which is defined as nausea and vomiting that persists despite preventive treatment recommended by ASCO or other guidelines.

The double-blind, randomized controlled trial compared olanzapine to metoclopramide, a drug often prescribed for breakthrough CINV although research has not been conducted to confirm its effectiveness for that purpose. Patients who received olanzapine did significantly better than the patients who received metoclopramide.

"This is the first time that breakthrough CINV has been studied in a systematic way," said Rudolph M. Navari, M.D., Ph.D., lead author of the study and professor of medicine, associate dean and clinical director of the Harper Cancer Institute, Indiana University School of Medicine-South Bend. "This study suggests that olanzapine will be very useful in these patients who feel very sick and sometimes come to the clinic, hospital or emergency room. As a result, patients will feel better."

Breakthrough CINV can lower the quality of life for cancer patients and can even necessitate reductions in their chemotherapy doses, possibly limiting the effectiveness of treatment. The study enrolled patients receiving highly emetogenic chemotherapy drugs, including cisplatin, doxorubicin and cyclophosphamide.

In the study, 205 patients who had never received chemotherapy were first given standard guideline-recommended drugs to prevent CINV prior to starting their chemotherapy. While these drugs prevented CINV in most of the patients, 80 patients developed breakthrough CINV. These patients were then randomized to receive either daily oral olanzapine or daily oral metoclopramide for three days. They were followed for 72 hours, through phone calls from study nurses, and were asked to fill out a diary.

During the 72-hour observation period, 71 percent (30 of 42) of those receiving olanzapine had no vomiting, compared to 32 percent (12 of 38) of those receiving metoclopramide. Sixty-seven percent (28 of 42) of the patients taking olanzapine experienced no nausea, compared with24 percent (9 of 38) of those taking metoclopramide.

While olanzapine, approved by FDA for treatment of psychosis, is known to cause a variety of side effects when taken daily for six months or longer, the short-term use in this study did not lead to any significant toxicities. Breakthrough CINV generally develops between the second to fourth days after chemotherapy treatment, so it would not be necessary to take olanzapine for longer than three days, Dr. Navari said. Olanzapine is relatively inexpensive and is taken orally.

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